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ISPH-0576

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

L. Cowser et al.

Appln. No. 09/854,883

Filed: May 14, 2001

For: ANTISENSE MODULATION OF  
PTP1B EXPRESSION

Assistant Commissioner for Patents  
Washington, DC 20231

) Group Art Unit: 1635

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) Examiner: J. Zara

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#13/TERM  
Disclaimed

TERMINAL DISCLAIMER UNDER 37 CFR § 1.321(c)

Sir:

Applicant hereby disclaims, except as provided below, that portion of the term of any patent issuing on the above-identified US Patent Application No. 09/854,883, which would extend beyond the term of any patent issuing on US Patent Application No. 09/629,644. Any patent granted on the above-identified US Patent Application No. 09/854,883 shall be enforceable only for and during such period that said patent is commonly owned with any patent granted on US Patent Application No. 09/629,644. This disclaimer shall run with any patent granted on the above-identified US Patent Application No. 09/854,883 and be binding upon its grantees, their successors and assigns.

This disclaimer will be null and void in the event that no patent issues on US Patent Application No. 09/629,644.

02/10/2003 HLE333 00000046 09854883

02 FC:1814

110.00 0P

Express Mail No. EU531797932US

Further, notwithstanding the above disclaimer, Applicant expressly does not disclaim that portion of the term of any patent issuing on US Patent Application No. 09/854,883 that would extend to the expiration date of any patent issuing on US Patent Application No. 09/629,644, in the event that the expiration date of any patent issued on the latter application is shortened by any of the following occurrences: (a) expiration due to failure to pay a maintenance fee; (b) the patent based on the latter application is held unenforceable; (c) the patent based on the latter application is found invalid by a court of competent jurisdiction; (d) the patent based on the latter application is statutorily disclaimed in whole or terminally disclaimed under 37 CFR §1.321; (e) the patent based on the latter application has all claims canceled by a reexamination certificate; (f) the patent based on the latter application is reissued; or (g) the patent based on the latter application is in any manner terminated prior to the expiration of its full statutory term as shortened by a terminal disclaimer filed prior to the grant of a patent thereon.

ISIS Pharmaceuticals, Inc., a corporation organized under the laws of the state of Delaware, and doing business at 2292 Faraday Avenue, Carlsbad, CA 92008, is the owner by assignment of the entire interest in and the above-identified US Patent Application No. 09/854,883 and co-owned US Patent Application No. 09/629,644.

The evidentiary documents relating to the ownership of the above-identified US Patent Application No. 09/854,883 and US Patent Application No. 09/629,644 and the inventions claims therein have been reviewed.

With respect to US Patent Application No. 09/629,644, this evidentiary document consists of an assignment by the six co-inventors of the subject matter of the invention to ISIS Pharmaceuticals, Inc. This assignment was executed by the co-inventors Lex M. Cowsert, Jacqueline Wyatt, Susan M. Freier, Brett P. Monia, Madeline M. Butler, and Robert McKay and assigned the co-inventors rights in the invention described in the US Patent Application No. 09/629,644 to ISIS Pharmaceuticals Inc. This assignment was forwarded for recordation on January 18, 2001. A copy of the assignment is attached.

With respect to the above-identified US Patent Application No. 09/854,883, the evidentiary documents consist of two (2) separate assignments conveying all rights in the invention described in the above-identified US Patent Application No. 09/854,883 and executed by co-inventors Lex M. Cowser and Jacqueline Wyatt in one instance, and by Susan M. Freier, Brett P. Monia, Madeline M. Butler, and Robert McKay in the other instance. These two assignments were recorded at Reel 012116, Frame 0470 and Reel 012116, Frame 0876. These assignments similarly conveyed the co-inventors rights in the present US Patent Application No. 09/854,883 to ISIS Pharmaceuticals, Inc. Copies of the recordation notices and assignments are attached.

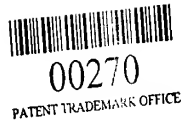
The undersigned attorney is an attorney of record in this application and to the best of my knowledge and belief, US Patent Application No. 09/629,644 and the above-identified US Patent Application No. 09/854,883 are commonly owned.

The appropriate filing fee under 37 CFR § 1.20(d) of \$55.00 is attached hereto. The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

HOWSON AND HOWSON  
Attorneys for Applicant

By Mary E. Bak  
Mary E. Bak  
Registration No. 31,215  
Spring House Corporate Center  
Box 457  
Spring House, PA 19477  
(215) 540-9200



ISPH-0576

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

L. Cowser et al.

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For: ANTISENSE MODULATION OF  
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RECEIVED  
FEB 12 2003  
TECH CENTER 1600/2900

Assistant Commissioner for Patents  
Washington, DC 20231

**TERMINAL DISCLAIMER UNDER 37 CFR § 1.321(c)**

Sir:

Applicant hereby disclaims that portion of the term of any patent issuing on the above-identified US Patent Application No. 09/854,883, which extends beyond the term of US Patent No. 6,261,840. This disclaimer shall run with any patent granted on the above-identified US Patent Application No. 09/854,883 and be binding upon its grantees, their successors and assigns. Any patent granted on the above-identified US Patent Application No. 09/854,883 shall be enforceable only for and during such period that said patent is commonly owned with US Patent No. 6,261,840.

ISIS Pharmaceuticals, Inc., a corporation organized under the laws of the state of Delaware, and doing business at 2292 Faraday Avenue, Carlsbad, CA 92008, is the owner by assignment of the entire interest in and to this US Patent Application No. 09/854,883 and co-owned issued US Patent No. 6,261,840.

Express Mail No. EU531797932US

The evidentiary documents relating to the ownership of US Patent No. 6,261,840 and the above-identified US Patent Application No. 09/854,883 and the inventions claimed therein have been reviewed.

With respect to US Patent No. 6,261,840, this evidentiary document consists of an assignment by the two co-inventors of the subject matter of the invention to ISIS Pharmaceuticals, Inc. This assignment was executed by co-inventors Lex M. Cowsert and Jacqueline Wyatt and assigned the co-inventors rights in the invention described in US Patent Application No. 09/487,368, which issued as US Patent No. 6,261,840, to ISIS Pharmaceuticals, Inc. This assignment was recorded at Reel 010552, Frame 0509. A copy of the recordation notice and assignment is attached.

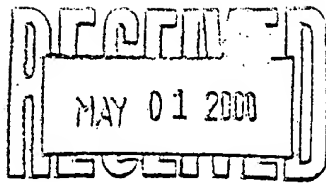
With respect to the above-identified US Patent Application No. 09/854,883, the evidentiary documents consist of two (2) separate assignments conveying all rights in the invention described in the above-identified US Patent Application No. 09/854,883 and executed by co-inventors Lex M. Cowsert and Jacqueline Wyatt in one instance, and by Susan M. Freier, Brett P. Monia, Madeline M. Butler, and Robert McKay in the other instance. These two assignments were recorded at Reel 012116, Frame 0470 and Reel 012116, Frame 0876. These assignments similarly conveyed the co-inventors rights in the present US Patent Application No. 09/854,883 to ISIS Pharmaceuticals, Inc. Copies of the recordation notices and assignments are attached.

The undersigned attorney is an attorney of record in this application and to the best of my knowledge and belief, US Patent No. 6,261,840 and the above-identified US Patent Application No. 09/854,883 are commonly owned.

The appropriate filing fee under 37 CFR § 1.20(d) of \$55.00 is attached hereto.  
The Director is hereby authorized to charge any deficiency in any fees due with the filing  
of this paper or credit any overpayment in any fees to our Deposit Account Number 08-  
3040.

Respectfully submitted,  
HOWSON AND HOWSON  
Attorneys for Applicant

By Mary E. Bak  
Mary E. Bak  
Registration No. 31,215  
Spring House Corporate Center  
Box 457  
Spring House, PA 19477  
(215) 540-9200



RTS-0093

UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark OfficeASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

APRIL 21, 2000-----

PTAS

JANE MASSEY LICATA  
66 EAST MAIN STREET  
MARLTON, NJ 08053

\*101270620A\*

UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 01/18/2000

REEL/FRAME: 010552/0509  
NUMBER OF PAGES: 4

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

COWSERT, LEX M.

DOC DATE: 01/06/2000

ASSIGNOR:

WYATT, JACQUELINE

DOC DATE: 01/06/2000

ASSIGNEE:

ISIS PHARMACEUTICALS INC  
2922 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09487368

FILING DATE: 01/18/2000

PATENT NUMBER:

ISSUE DATE:

ANNE HARRELL, PARALEGAL  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

DOCUMENTATION DATE: 01/18/2000

REEL/FRAME: 010552/0509  
PATENT/APP: 09487368/0000

A S S I G N M E N T

WHEREAS, we Lex M. Cowsert, residing at 3008 Newshire Street Carlsbad CA 92008 and Jacqueline Wyatt, residing at 1065 Hymettus Avenue Encinitas CA 92024 hereinafter referred to as the assignors, are the joint inventors of certain inventions or improvements for which we have made application for Letters Patent to the United States, identified as Case No. RTS-0093 entitled **Antisense Modulation of PTP1B Expression**; filed concurrently herewith; and

WHEREAS, **Isis Pharmaceuticals Inc.** hereinafter referred to as the assignee, of **2922 Faraday Ave, Carlsbad, California 92008** is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers, to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

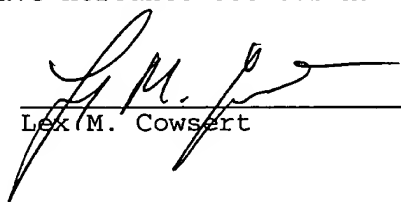


AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

We further authorize and direct our attorneys to insert below\* the serial number and filing date of said application now identified as Case No. RTS-0093 as soon as the same shall have been made known to them by the United States Patent Office.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

Dated: 1/4/00

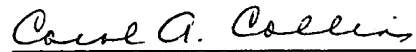
  
Lex M. Cowser

STATE OF CALIFORNIA     )  
                                  ) ss.  
COUNTY OF SAN DIEGO    )

This 4<sup>th</sup> day of JANUARY, 2000, before me personally came the above-named Lex M. Cowser, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/she executed the same of his/her own free will for the purposes set forth therein.



[SEAL]

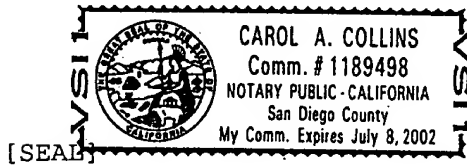
  
Notary Public for CALIFORNIA  
My commission expires: 7/8/02

Dated: 1/6/00

Jacqueline R Wyatt  
Jacqueline Wyatt

STATE OF CALIFORNIA )  
COUNTY OF SAN DIEGO ) ss.

This 6<sup>th</sup> day of JANUARY, 2000, before me personally came the above-named Jacqueline Wyatt, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/she executed the same of his/her own free will for the purposes set forth therein.



Carol A. Collins  
Notary Public for CALIFORNIA  
My commission expires: 7/8/02



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

NOVEMBER 01, 2001

PTAS



\*101830757A\*

HOWSON AND HOWSON  
MARY E. BAK, ESQUIRE  
SPRING HOUSE CORPORATE CENTER  
BOX 457  
SPRING HOUSE, PENNSYLVANIA 19477

**UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT**

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PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 08/29/2001

REEL/FRAME: 012116/0876  
NUMBER OF PAGES: 7

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

WYATT, JACQUELINE

DOC DATE: 07/19/2001

ASSIGNOR:

FREIER, SUSAN M.

DOC DATE: 07/30/2001

ASSIGNOR:

MONIA, BRETT P.

DOC DATE: 07/31/2001

ASSIGNOR:

BUTLER, MADELINE M.

DOC DATE: 08/14/2001

ASSIGNOR:

MCKAY, ROBERT

DOC DATE: 08/13/2001

ASSIGNEE:

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

012116/0876 PAGE 2

SERIAL NUMBER: 09854883  
PATENT NUMBER:

FILING DATE: 05/14/2001  
ISSUE DATE:

ALLYSON PURNELL, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

## A S S I G N M E N T

WHEREAS, We, Lex M. Cowsert, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, <sup>ENCINITAS</sup> of ~~La Costa~~, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Lex M. Cowsert

State of California        )  
                                  )    ss.  
County of San Diego        )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowsert, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

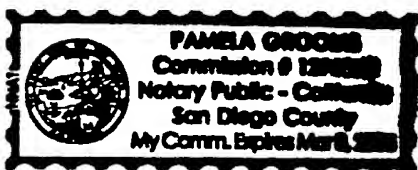
WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: 4/17, 2001Jacqueline R Wyatt  
Jacqueline Wyatt

State of California       )  
                                  ) ss.  
County of San Diego     )

On this 19<sup>th</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

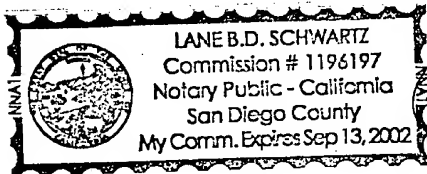
Pamela Groves  
Signature of Notary

DATED: July 30, 2001

Susan Freier  
Susan M. Freier

State of California       )  
                                  ) ss.  
County of San Diego     )

On this 30<sup>th</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/proved to me on the basis of ~~satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Lane B.D. Schwartz  
Signature of Notary

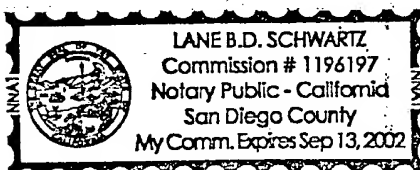


DATED: 7/31, 2001

Brett P. Monia  
Brett P. Monia

State of California )  
 ) ss.  
County of San Diego )

On this 31<sup>st</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

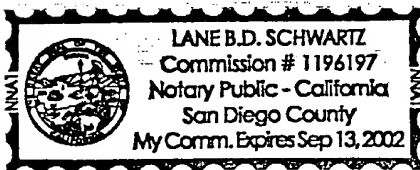
Lane B.D. Schwartz  
Signature of Notary

DATED: 8/14, 2001

Madeline M. Butler  
Madeline M. Butler

State of California )  
 ) ss.  
County of San Diego )

On this 14 day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



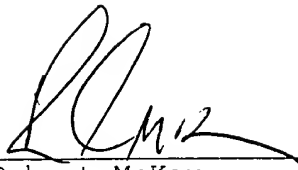
WITNESS my hand and official seal.

Lane B.D. Schwartz  
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

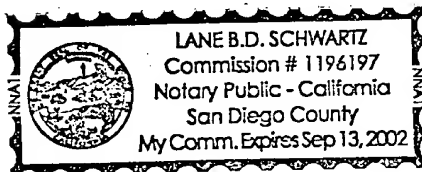
DATED: 8-13-01, 2001

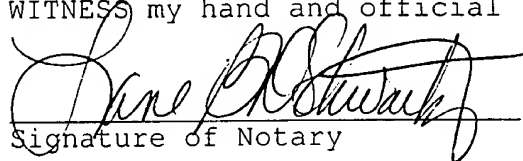
  
Robert McKay

State of California       )  
                                      ) ss.  
County of San Diego       )

On this 13<sup>th</sup> day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



  
Signature of Notary



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

NOVEMBER 08, 2001

PTAS



\*101830716A\*

HOWSON AND HOWSON  
MARY E. BAK, ESQ.  
SPRING HOUSE CORPORATE CENTER  
BOX 457  
SPRING HOUSE, PA 19477

**UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT**

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 08/29/2001

REEL/FRAME: 012116/0470  
NUMBER OF PAGES: 7

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

**ASSIGNOR:**

COWSERT, LEX M.

DOC DATE: 07/30/2001

**ASSIGNEE:**

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09854883  
PATENT NUMBER:

FILING DATE: 05/14/2001  
ISSUE DATE:

JEEVON JONES, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

## A S S I G N M E N T

WHEREAS, We, Lex M. Cowsert, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, of ~~La Costa~~ <sup>ENCINITAS</sup>, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

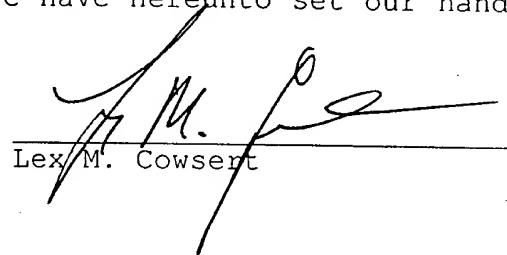
result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: 7/30, 2001

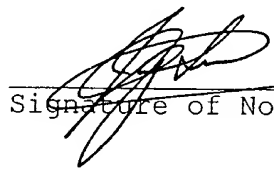
  
Lex M. Cowser

State of California )  
County of San ~~Diego~~ <sup>MATEO</sup> ) ss.

On this 30<sup>TH</sup> day of JULY, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowser, ~~personally known to me~~ proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Jacqueline Wyatt

State of California       )  
                                  )   ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Susan M. Freier

State of California       )  
                                  )   ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Brett P. Monia

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Madeline M. Butler

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary



DOCKET NO.: ISPH-0576

PATENT

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Robert McKay

State of California     )  
                              )   ss.  
County of San Diego     )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

## A S S I G N M E N T

WHEREAS, We, Lex M. Cowser, of Carlsbad, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, of La Costa, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1B Expression, for which we have made application for Letters Patent of the United States, said application having been filed July 31, 2000 and assigned Application No. 09/629,644; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

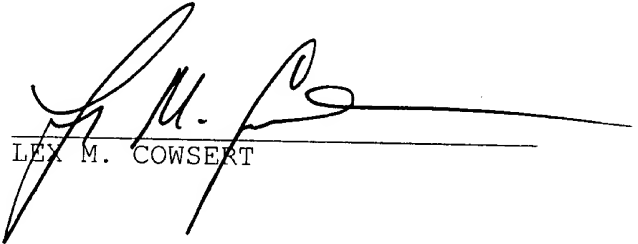
DOCKET NO.: ISPH-0478

PATENT

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

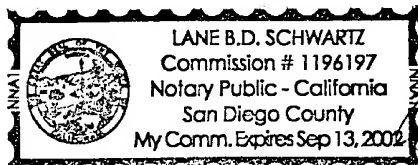
IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: 10/30, 2000

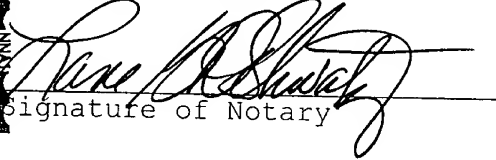
  
LEX M. COWSERT

State of California       )  
                                  ) ss.  
County of San Diego       )

On this 30<sup>th</sup> day of October, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowsert, personally known to me/~~proved to me on the basis of satisfactory evidence to be~~ the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



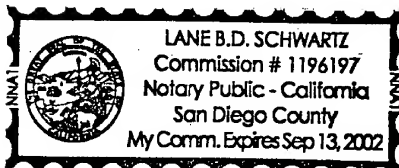
WITNESS my hand and official seal.

  
Signature of Notary

DATED: 11/1, 2000Jacqueline R. Wyatt  
JACQUELINE WYATT

State of California     )  
                                  )     ss.  
County of San Diego     )

On this 1st day of November, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.


Lane B.D. Schwartz  
Signature of NotaryDATED: 30-Oct, 2000Susan M. Freier  
SUSAN M. FREIER

State of California     )  
                                  )     ss.  
County of San Diego     )

On this 30th day of October, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Carol A. Collins  
Signature of Notary

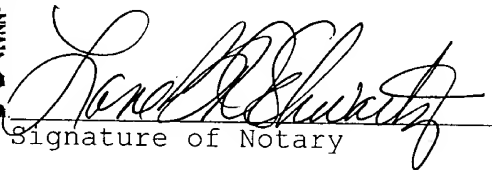
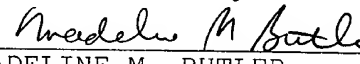
DATED: 11/15, 2000
  
 BRETT P. MONIA

State of California )  
 ) ss.  
 County of San Diego )

On this 15th day of November, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

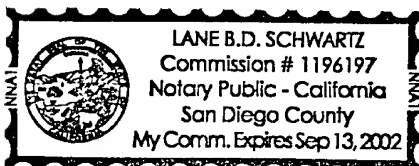


WITNESS my hand and official seal.

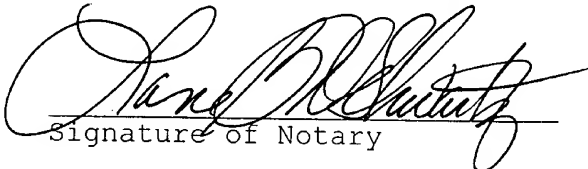
  
 Signature of Notary
DATED: 10/30, 2000
  
 MADELINE M. BUTLER

State of California )  
 ) ss.  
 County of San Diego )

On this 30th day of October, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

  
 Signature of Notary

DOCKET NO.: ISPH-0478

PATENT

DATED: 10/27, 2000

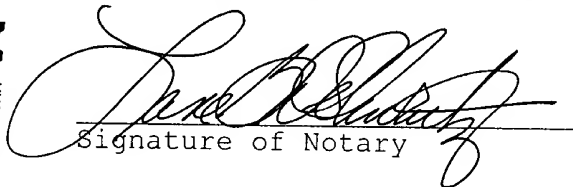
  
ROBERT MCKAY

State of California       )  
                                  ) ss.  
County of San Diego       )

On this 27<sup>th</sup> day of October, 2000, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



  
Signature of Notary



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

NOVEMBER 01, 2001

PTAS

HOWSON AND HOWSON  
MARY E. BAK, ESQUIRE  
SPRING HOUSE CORPORATE CENTER  
BOX 457  
SPRING HOUSE, PENNSYLVANIA 19477



\*101830757A\*

UNITED STATES PATENT AND TRADEMARK OFFICE  
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RECORDATION DATE: 08/29/2001

REEL/FRAME: 012116/0876  
NUMBER OF PAGES: 7

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

WYATT, JACQUELINE

DOC DATE: 07/19/2001

ASSIGNOR:

FREIER, SUSAN M.

DOC DATE: 07/30/2001

ASSIGNOR:

MONIA, BRETT P.

DOC DATE: 07/31/2001

ASSIGNOR:

BUTLER, MADELINE M.

DOC DATE: 08/14/2001

ASSIGNOR:

MCKAY, ROBERT

DOC DATE: 08/13/2001

ASSIGNEE:

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008



012116/0876 PAGE 2

SERIAL NUMBER: 09854883  
PATENT NUMBER:

FILING DATE: 05/14/2001  
ISSUE DATE:

ALLYSON PURNELL, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

## A S S I G N M E N T

WHEREAS, We, Lex M. Cowsert, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, <sup>ENCINITAS</sup> of ~~La Costa~~, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

DOCKET NO.: ISPH-0576

PATENT

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Lex M. Cowser

State of California        )  
                                  )    ss.  
County of San Diego        )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowser, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

DATED: 4/12, 2001

Jacqueline R Wyatt  
Jacqueline Wyatt

State of California )  
 ) ss.  
County of San Diego )

On this 19<sup>th</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

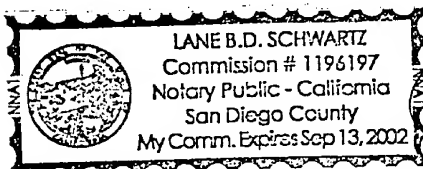
Pamela Groome  
Signature of Notary

DATED: July 30, 2001

Susan M. Freier  
Susan M. Freier

State of California )  
 ) ss.  
County of San Diego )

On this 30<sup>th</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Lane B.D. Schwartz  
Signature of Notary

DOCKET NO.: ISPH-0576

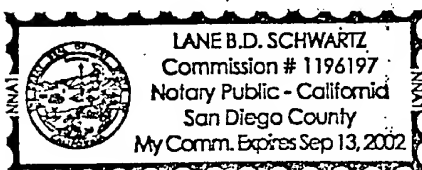
PATENT

DATED: 7/31, 2001

Brett P. Monia  
Brett P. Monia

State of California )  
County of San Diego ) ss.

On this 31<sup>st</sup> day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

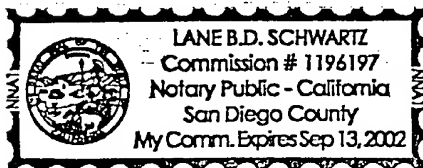
Lane B.D. Schwartz  
Signature of Notary

DATED: 8/14, 2001

Madeline M. Butler  
Madeline M. Butler

State of California )  
County of San Diego ) ss.

On this 14 day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



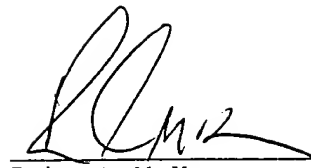
WITNESS my hand and official seal.

Lane B.D. Schwartz  
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

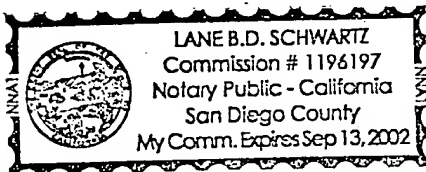
DATED: 8:13.01, 2001

  
Robert McKay

State of California     )  
                                  )     ss.  
County of San Diego     )

On this 13<sup>th</sup> day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



  
Signature of Notary



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

ASSISTANT SECRETARY AND COMMISSIONER  
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Washington, D.C. 20231

NOVEMBER 08, 2001

PTAS



\*101830716A\*

HOWSON AND HOWSON  
MARY E. BAK, ESQ.  
SPRING HOUSE CORPORATE CENTER  
BOX 457  
SPRING HOUSE, PA 19477

**RECEIVED**

**FEB 12 2003**

**UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT**

**TECH CENTER 1600/2900**

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 08/29/2001

REEL/FRAME: 012116/0470  
NUMBER OF PAGES: 7

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

**ASSIGNOR:**

COWSERT, LEX M.

DOC DATE: 07/30/2001

**ASSIGNEE:**

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09854883  
PATENT NUMBER:

FILING DATE: 05/14/2001  
ISSUE DATE:

JEEVON JONES, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS



## A S S I G N M E N T

WHEREAS, We, Lex M. Cowsert, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, of ~~La Costa~~ <sup>ENCINITAS</sup>, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

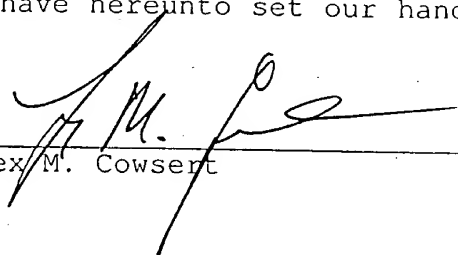
result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

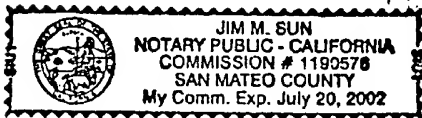
DATED: 7/30, 2001

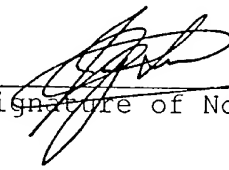
  
Lex M. Cowser

State of California                    )  
  ) ss.  
County of San ~~Diego~~ <sup>MATEO</sup> )

On this 30<sup>TH</sup> day of JULY, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowser, ~~personally known to me~~ proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



  
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Jacqueline Wyatt

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Susan M. Freier

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Brett P. Monia

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Madeline M. Butler

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

DATED: \_\_\_\_\_, 2001

\_\_\_\_\_  
Robert McKay

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary